in the brain in anaesthetized animals by passing DC current of 4 mA for 30 sec through the implanted electrodes. The brain was then perfused with 10% formalin and histopathological verification of the electrodes site was confirmed subsequently.

Results and discussion. In the present study, serum from monkeys after the electrical stimulation of the LHA, VMH, Po and CC were investigated for their insulin content. The table shows a significant increase in IRI following LHA stimulation. Expressing the prestimulation basal IRI (0 min) as 100%, the mean IRI at 10, 20, 30, 120 and 210 min was +121%, +120%, +154%, +214% and +112% respectively. An opposite response was obtained from VMH; the corresponding mean IRI values were −82.6%, −86.8%, −76.0%, −67.0% and −62.0% respectively. The stimulation of control electrode in the CC as well as that in the Po area did not result in any significant change in the levels of IRI. The functional reciprocity between 'feeding' (LHA) and 'satiety' (VMH) areas was also observed in the case of insulin, in addition to the reciprocity in feeding behaviour. Thus, insulinogenic and insulinoprival responses were obtained following the stimulation of 'feeding' and 'satiety' centres in the hypothalamus, suggesting a significant role of insulin in the regulation of food intake.

Idahl and Martin[13] and Martin et al.[14] reported that mouse ventrolateral hypothalamus releases a humoral factor in vitro which stimulates insulin secretion from islets of Langerhans. The extract from LHA stimulated, while that from VMH inhibited insulin secretion. Our results (in vivo) find support from those performed in vitro by Idahl and Martin[13] and Martin et al.[14]. Thus our findings suggest a close relationship between feeding behaviour and insulin secretion.

1 Present address: S.K.G., Lecturer in Biochemistry, Department of Biology, Guru Nanak Dev University, Amritsar-143005 (India).
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CNS stimulation effect on the sexual maturation of the female rat[1]

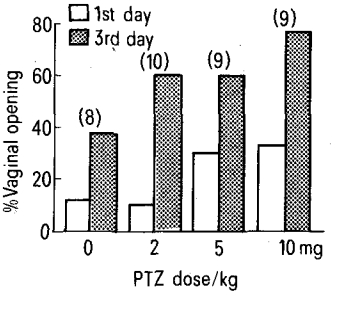
A.D. Okonmah[2] and K.F.A. Soliman[3]

Florida A and M University, School of Pharmacy, Tallahassee (Florida 32307, USA), 23 February 1978

Summary. In the immature rat, CNS stimulants administration to pregnant mare serum gonadotropin (PMSG) primed rats resulted in significant ($p < 0.01$) ovarian and uterine hypertrophy when compared to animals treated with PMSG only. Meanwhile precocious puberty was produced by pentylenetetrazol treatment alone. The results of this experiment may indicate that administration of CNS stimulants has a specific action on the release of endogenous gonadotropin.

The involvement of the CNS in sexual puberty has been recognized for many years[4]. The immature hypophysis has been shown to contain significant quantities of gonadotropins, however, this gonadotropin is secreted in limited quantities during prepubertal life; hence the immature pituitary is capable of supporting reproductive function prior to the puberty[5]. It has been documented that hippocampus or pyriform lobe damaged during infancy (1 week) caused diminished gonadol development[6]. Precocious puberty was also recorded following the neural isolation of the medial basal hypothalamus[7]. Meanwhile, testosterone administration was found to induce precocious puberty in the female rat. This effect has been shown to be mediated by the hippocampus[8]. Recently, neural excitation with amino acids has been implicated in the regulation of gonadotropin secretion and the control of reproductive function in man[9]. The purpose of this investigation was to illustrate the effect of various CNS stimulant drugs on the hypertrophy of the ovary and uterus following the administration of PMSG and/or testosterone to the female immature rats.

Methods. Immature female Sprague Dawley rats with an average b.wt of 50–60 g were obtained from the Southern Animal farms, Alabama, at the age of 22 days. They were maintained on a 14 h:10 h light: dark cycle, with a controlled temperature of 23±1 °C and were fed with Purina rat chow and water ad libitum. In the 1st study, 8 groups of rats were utilized; each group was made up of 8 rats. Treatment was begun at the age of 23 days for the period of 3 days. Pregnant mare serum gonadotropin (20 IU PMSG, Sigma), theophylline (10 mg/kg, Nutritional Biochemical Corporation), picrotoxin (5 mg/kg, Pfaltz and Bauer, Inc.), testosterone (Δ^4-androsten-17B-o1-3 one; 5 mg/kg; Sigma) and pentylenetetrazol (pentamethylene-



Effect of 0 mg, 2 mg, 5 mg, and 10 mg/kg of pentylenetetrazol treatment on vaginal opening. Numbers within the bars indicated number of animals used.

Effect of CNS stimulation on reproductive organs of PMSG-treated immature rats

Treatment	Body wt	Ovarian wt	Uterine wt
Control	69.6 ± 1.2[a]*	52.4 ± 4.1[a]	91.2 ± 12.1[a]
PMSG	75.3 ± 1.5[a]	149.6 ± 13.9[b]	158.7 ± 16.8[b]
Testosterone	73.5 ± 2.5[a]	42.8 ± 4.2[a]	214.5 ± 15.6[c]
PMSG + testosterone	72.8 ± 3.2[a]	176.2 ± 2.5[b]	329.5 ± 15.3[d]
PMSG + testosterone theophylline	70.5 ± 6.0[a]	198.1 ± 1.9[c]	337.8 ± 12.3[d]
PMSG + testosterone picrotoxin	74.5 ± 2.1[a]	170.5 ± 7.5[b]	266.0 ± 11.2[cd]
PMSG + testosterone + pentylenetetrazol	72.5 ± 3.7[a]	258.8 ± 1.9[d]	367.0 ± 13.5[d]
PMSG + pentylenetetrazol	68.0 ± 5.9[a]	200.6 ± 5.8[c]	197.8 ± 19.0[c]

*Means with the same Superscript are not significantly different ($p > 0.05$).

tetrazol, 10 mg/kg, PTZ, Knoll Pharmaceutical Co, New Jersey), were utilized in this study. At the end of the treatment, all animals were sacrificed using ether, and the uterus and ovaries were removed, cleaned, weighed and recorded.

In the 2nd study, a total of 40 rats were used. There were 10 rats in a group. Treatment started at the age of 27 days. 2 mg, 5 mg and 10 mg/kg of PTZ was administered i.p. for 3 days while saline, the drug vehicle, was administered to the control group for the same length of time. Examination of the vaginal opening was resumed a day after the drug treatment was terminated. The number of animals with opened vagina on the 1st and the 3rd day was recorded. Data were subjected to 1-way analysis of variance and F test and SE of the means was determined.

Results. The table shows the hypertrophic effect which was noticed in the ovarian and the uterine tissues of animals treated with PMSG. The administration of 5 mg/kg of testosterone resulted in a significant ($p < 0.01$) change in the uterine weight. Administration of PTZ, theophylline and picrotoxin to the PMSG- and testosterone-treated animals resulted in a significant ($p < 0.05$) hypertrophy of the ovaries, but the uterine weight was not significantly ($p > 0.05$) different from PMSG-treated group. Administration of 10 mg/kg PTZ to the PMSG-treated animals resulted in a significant increase ($p < 0.01$) in ovarian weight when compared to the rest of the treatments, with the exceptions of the theophylline-treated group. The ovarian weight changes produced by testosterone was not significantly different from control but the difference was significant ($p < 0.01$) when the uteri from testosterone-treated animals were compared to control group. There was no change in the average body weight among all treatments. The figure shows the percentage of animals with vaginal openings with 3 different dosages of PTZ treatment. 3 daily doses of 2 mg, 5 mg and 10 mg/kg of PTZ induced a dose related increase in vaginal openings. There was more than 100% increase in vaginal openings with 10-mg-treated group when compared to the control group.

Discussion. The ovarian hypertrophy noticed using PMSG treatment has been documented previously to be the result of the direct action of the gonadotropin on the ovary[10,11]. Meanwhile the uterine hypertrophy that resulted in the PMSG-treated group may have been mediated through PMSG stimulation of ovarian estrogen production[10,11]. When 5 mg/kg of testosterone was administered to the PMSG-treated animals, there was a noticeable change in ovarian and uterine weight. However, when testosterone was administered alone, there was no change in the ovarian weight, but a significant hypertrophy of the uterus was noticed. Testosterone seems to have potentiative effect on the ovaries and uteri of the PMSG-treated theophylline, picrotoxin- and PTZ-treated group. However, the actual mechanism by which testosterone may have brought about this physiological change is yet to be explained, but recently, it has been indicated that testosterone effect on the uterus may be brought by the ability of the ovary to transfer testosterone to estrogen[12]. The use of CNS stimulant drugs in the PMSG- and testosterone-treated animals may also suggest a potentiative effect noticed with the increase in the ovarian and uterine weights. The ovarian hypertrophy noticed may be the result of possible release of endogenous gonadotropin. PTZ is known as a CNS stimulant drug which has been widely studied in man and experimental animals[13]. The actions of the drug are exerted primarily on the CNS[13]. All levels of the cerebrospinal axis are stimulated by the drug[13]. The CNS stimulating effect of PTZ was attributed recently[14] to its selective blockade of gamma amino butyric acid (GABA) mediated inhibition. Since the action of PTZ, picrotoxin and theophylline are known to affect the CNS, though with different mechanism of actions, it may be suggested that during the CNS stimulatory action of these drugs, area of the hypothalamus, specifically the arcurate nucleus controlling the tonic release of gonadotropin may have been affected[15,16]. Moreover, there was some evidence that gonadotropin surge could be blocked by CNS blocking agents[10]. Further evidence that PTZ enhance the sexual puberty of the female immature rat is indicated by studying the vaginal openings of PTZ-treated animals. In this study a dose response relationship was obtained. It is concluded from these experiments that PTZ effect on the ovary and the uterus may be mediated through the probable release of endogenous gonadotropin.

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2 National Institute of Health, MBS Graduate Trainee.
3 To whom request for reprints should be addressed.
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